

November 4, 1999

VETERINARY SERVICES MEMORANDUM NO. 800.94

Subject: FDA Export Reform and Enhancement Act of 1996

To: Biologics Licensees, Permittees, and Applicants
Directors, Center for Veterinary Biologics

I. PURPOSE

This memorandum provides guidance to licensees, permittees, and applicants concerning Animal and Plant Health Inspection Service (APHIS) implementation of the FDA Export Reform and Enhancement Act of 1996 (FDA-EREA), Section 802 (21 U.S.C. 382), as it applies to veterinary biological products.

II. BACKGROUND

The FDA-EREA signed by President Clinton April 26, 1996, allows the export of certain drugs, biologicals, animal drugs, and medical devices, that are not approved for distribution and sale in the United States, to any country in the world if they are in compliance with the laws of the importing country and have been approved for marketing in a country listed in the FDA-EREA. The FDA-EREA defines the term “drug” to include veterinary biological products which require licensing by the Secretary of Agriculture under the Virus Serum Toxin Act of 1913 (VST Act). The VST Act requires preparation of all veterinary biological products shipped in or from the United States, under and in compliance with USDA regulations, at a USDA licensed establishment. The FDA-EREA, however, supersedes these requirements and under certain conditions permits preparation of certain veterinary biological products that are not licensed by USDA for export. The following guidelines describe how APHIS will apply the provisions of the FDA-EREA that apply to the production and export of veterinary biological products that are not approved (unlicensed) for distribution and sale in the United States.

III. GUIDELINES

The FDA-EREA is composed of two sections (801 & 802). Section 801 concerning imports for exports, is not applicable to veterinary biological products. Section 802, however, concerning exports of certain unapproved products, applies to all veterinary biological products that require licensing under the VST Act. This includes all products that meet the definition of “biological products” in 9 CFR 101.2.

A. Provisions of the FDA-EREA

The following is a summary of the provisions of Section 802 of the FDA-EREA that apply to veterinary biological products. This summary includes references to the applicable sections of the FDA-EREA which is available on the Internet at http://www.fda.gov/ora/import/impexp/ora_impexp_sec.html.

1. *Export to Any Country* - A person may export an unlicensed veterinary biological product to any country so long as the product complies with the laws of the import country and the exporter has a marketing authorization for the product from the appropriate authority in Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, the European Union, or a country in the European Economic Area.

Reference: 802(b)(1)(A)

2. *Notification to Center for Veterinary Biologics-Licensing and Policy Development (CVB-LPD)* - If a person produces the product in facilities that are not licensed by USDA and export is to one of the countries specifically listed in 802(b)(1)(A), simple notification to CVB-LPD identifying the unlicensed veterinary biological product the person is exporting is all that is necessary.

Reference: 802(g)

a. If the import country is not one of the countries specifically listed in 802(b)(1)(A), notification to CVB-LPD must include the name of the country to which the person is exporting the veterinary biological product, the identity of the veterinary biological product, and documentation as appropriate according to sections III. A. 5. or 6. of this memorandum.

b. If a person plans to produce an unlicensed product in a USDA-licensed veterinary biologics establishment for export under the FDA-EREA, notification to CVB-LPD should also include a request for authorization to produce unlicensed product in a licensed production facility in accordance with section III. B. of this memorandum.

3. *Maintain Records* - Any exporter of a veterinary biological product under the provisions of the FDA-EREA must maintain records of all such products exported and the countries to which they were exported.

Reference: 802(g)

4. *Prohibited From Export* - A person may not export an unlicensed veterinary biological product under the FDA-EREA if the product:

a. Does not conform with current good manufacturing practice (GMP) requirements or other international standards recognized by the Secretary of Agriculture in its manufacturing, processing, packaging, and holding.

Reference: 802(f)(1)

b. Is otherwise adulterated as defined in section 501 of the Food Drug and Cosmetic Act (21 U.S.C. 381).

Reference: 802(f)(2)

c. Does not fulfill the requirements of section 801(e)(1)(A) through (D) of the FDA-EREA which states that a product is not deemed misbranded if the product:

(1) Accords with the specifications of the foreign purchaser.

(2) Is not in conflict with the laws of the country to which it is intended for export.

(3) Is labeled on the outside of the shipping package that it is intended for export.

(4) Is not sold or offered for sale in domestic commerce.

Reference: 802(f)(3)

d. Presents an imminent hazard to the health and safety of the United States.

Reference: 802(f)(4)(A)

e. Presents an imminent hazard to the public health of the country to which the product would be exported.

Reference: 802(f)(4)(B)

f. Is not labeled in accordance with the requirements and conditions for use in both the country that has granted the marketing authorization for the product and the country to which the product would be exported.

Reference: 802(f)(5)(A)

g. Is not labeled in the language and units of measurement of the country to which the product would be exported or in the language designated by such country.

Reference: 802(f)(5)(B)

h. Is not promoted in accordance with the labeling requirements set forth in 802(f)(5).

Reference: 802(f)(6)

5. *Additions to the List of Approved Countries* - Countries can be added to the list of countries in 802(b)(1)(B).

a. The appropriate country official, manufacturer, or exporter may request the Secretary of Agriculture to take action under 802(b)(1)(B) by submitting documentation to CVB-LPD in support of such designation.

b. If a person other than the appropriate country official requests such designation, a letter from the appropriate country official indicating the desire of such country to be so designated must accompany the request.

Reference: 802(b)(1)(C)

c. The Secretary of Agriculture may designate an additional country to be included in the list of countries in 802 (b)(1)(A) if :

(1) The country has statutory authority to review the safety and effectiveness of veterinary biological products by experts based upon the evaluation of adequate and well controlled investigations and only approves the marketing of products which have been determined to be safe and effective.

Reference: 802(b)(1)(B)(i)

(2) The country has statutory requirements that ensure the methods, facilities, and controls used for the manufacture, processing, and packing of veterinary biological products are adequate to preserve their identity, quality, purity, and strength.

Reference: 802(b)(1)(B)(ii)

(3) The country has statutory requirements for the reporting of adverse reactions related to the use of veterinary biological products and for procedures which it follows to withdraw approval of unsafe or ineffective products.

Reference: 802(b)(1)(B)(iii)

(4) The country has statutory requirements that labeling and promotion of veterinary biological products are in accordance with the approval of the product.

Reference: 802(b)(1)(B)(iv)

(5) The country has a valid marketing authorization system that is equivalent to the systems in the countries described in 802(b)(1)(A).

Reference: 802(b)(1)(B)(v)

6. *Export to Countries Not Listed in the FDA-EREA* - Persons may export unlicensed veterinary biological products to a country which is not listed in 802(b)(1)(A) if :

a. The product complies with the laws of the import country and has a valid marketing authorization by the responsible authority in that country.

Reference: 802(b)(2)(A)

b. The Secretary of Agriculture determines (based on documentation submitted to CVB-LPD) that all of the following requirements are met in that country:

Reference: 802(b)(2)(B)

(1) The importing country has statutory authority to review the safety and effectiveness of veterinary biological products by experts based upon the evaluation of adequate and well controlled investigations and only approves the marketing of products which have been determined to be safe and effective.

Reference: 802(b)(2)(B)(i)

(2) The importing country has statutory requirements that ensure the methods, facilities, and controls used for the manufacture, processing, and packing of veterinary biological products are adequate to preserve their identity, quality, purity, and strength.

Reference: 802(b)(2)(B)(ii)

(3) The importing country has statutory requirements for the reporting of adverse reactions related to the use of veterinary biological products and for procedures which it follows to withdraw approval of unsafe or ineffective products.

Reference: 802(b)(2)(B)(iii)

(4) The importing country has statutory requirements that labeling and promotion of veterinary biological products are in accordance with the approval of the product.

Reference: 802(b)(2)(B)(iv)

7. *Products Not Meeting the Provisions of the FDA-EREA* - APHIS can allow the export of a veterinary biological product described in 802(a) which would not meet the conditions for approval under the FDA-EREA or conditions for approval of a country described in 802(b)(1)(A) or 802(b)(2) if the exporter petitions APHIS. APHIS must take action within 60 days of receipt of a petition sent to CVB-LPD containing the following:

a. Certification by the person exporting the product that the veterinary biological product would not meet the conditions for approval of a country described in 802(b)(1)(A),

Reference: 802(b)(3)(B)

b. Credible evidence that the veterinary biological product would be safe and effective under the conditions of use in the country to which it is being exported, and

Reference: 802(b)(3)(A)

c. A request for approval of the export of the product from the appropriate animal health authority in the importing country certifying that it is understood that APHIS has not approved the veterinary biological product for export under the FDA-EREA and concurring that the scientific evidence that the product would be reasonably safe and effective is credible.

Reference: 802(b)(3)(B)

8. *Export of Investigational Products* - A person may export an investigational product (produced in a licensed establishment according to 9 CFR 103.1 or in an unlicensed establishment that conforms to GMP or other recognized international standard) to a country listed in 802(b)(1)(A) in accordance with the laws of that country.

Reference: 802(c)

9. *Export in Anticipation of Marketing Authorization* - A person may export a product intended for formulation, filling, packaging, labeling, or further processing in anticipation of marketing authorization in any country listed in section (b)(1)(A) in accordance with the laws of that country.

Reference: 802(d)

10. *Products for Tropical Diseases or Diseases not of Significant Prevalence in the United States* - Veterinary biological products for tropical diseases or other diseases not of significant prevalence in the United States and which do not otherwise qualify for export under the FDA-EREA, may also be permitted to be exported under certain conditions provided production of the product in the United States does not endanger the livestock and poultry of the United States.

Reference: 802(e)

B. Production of Unlicensed Veterinary Biological Products in USDA Licensed Veterinary Biologics Establishments for Export Under the FDA-EREA

The regulations in 9 CFR 114.2 prohibit the production of unlicensed veterinary biological products in USDA licensed veterinary biologics establishments except for experimental products authorized according to 9 CFR 103.1 and for State licensed products produced under exemption from license according to 9 CFR 107.2. Regulations in 9 CFR 114.2 prohibit production of unlicensed products in licensed production facilities unless authorized by CVB-LPD in accordance with 9 CFR 114.1. CVB-LPD may authorize an establishment to produce an unlicensed product in licensed production facilities if such production does not result in a risk of contamination of licensed products or a risk to the health of U.S. livestock or poultry.

1. *Authorization to Produce Unlicensed Products* - CVB-LPD may authorize the production of unlicensed products in USDA licensed establishments for export under the FDA-EREA provided the establishment:

a. Produces such unlicensed products only for export under the FDA-EREA, the products' labeling does not bear a U.S. Veterinary Biologics Establishment License Number, and the exporter does not otherwise represent the product in any manner as having met the requirements for licensure.

b. Prepares all products, whether licensed or unlicensed, in locations indicated in blueprints and legends filed in accordance with 9 CFR 108. Center for Veterinary Biologics-Inspection and Compliance may conduct an inspection of the production facilities prior to filing such amended blueprints and legends to ensure production of the unlicensed product(s) does not pose a risk of contamination to licensed products or a risk to the health of U.S. livestock or poultry.

c. Prepares an Outline of Production in accordance with 9 CFR 114.9, for each unlicensed product. CVB will not stamp such outlines as "filed", but will review them to assure they provide an adequate description of the method of production.

d. Appropriately tests the Master Seeds, Master Cell Stocks, and ingredients used in the production of the unlicensed product to ensure freedom from contamination with bacteria, fungi, mycoplasma, viruses, and other agents in accordance with 9 CFR 113 or other acceptable national standards.

e. Fully characterizes and identifies Master Seeds and Master Cell Stocks used in the production of the unlicensed product as indicated in the Outline of Production.

f. Maintains records in accordance with 9 CFR 116.1 and 116.2 that include all products whether licensed or unlicensed.

g. Submits reports prescribed in 9 CFR 116.5 for all products whether licensed or unlicensed.

2. *Licensing of Products Produced Under the FDA-EREA* - If authorized by CVB-LPD, a person may produce unlicensed products for export under the FDA-EREA in a USDA licensed Establishment even though the person is not pursuing a U.S. Veterinary Biological Product License for the product. However, if the person applies for and CVB-LPD issues such a license, production and export of the unlicensed product in the person's licensed establishment under the FDA-EREA must stop on the date CVB-LPD issues the product license.

/s/ Thomas E. Walton for

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